Remarks

Status of the Claims

Claims 1-112 are canceled and new claims 113-149 are added herein. Claims 113-149 are pending in the application.

Support for the nucleic acid molecule of claim 113, is found, *inter alia*, in Figures 4A, 8B, and 8I. For example the plasmid pEZC1003 shown in Figure 4A. The pEZC1003 plasmid comprises, in order, an origin of replication, a first positive selection marker (kan), a promoter (a T7 promoter), a first site-specific recombination site (an *att*P site), a second positive selection marker (CAM), a second site-specific recombination site (a *lox*P site), and a second promoter (SP6).

The pEZC3501 plasmid contains a promoter (the pTac promoter), a protein coding region (GST), and a site-specific recombination site (an *att*R1 site). This configuration is designed for the introduction or a coding sequence and is designed to generate, after recombination, vector which encode a fusion protein and is supported, *inter alia*, in the '291 application at page 27, lines 3-12; page 28, lines 6-9; and page 30, lines 24-28.

Figure 4E shows a product vector of a recombination reaction which contains, in order, a promoter (SP6), a site-specific recombination site (a *lox*P site), and a positive selection marker (Cam), generated as described in Example 2 of the '291 application.

Support for the nucleic acid molecule of claim 125, is found, *inter alia*, in Figure 8B, for example the plasmid pEZC3501. The pEZC3501 plasmid comprises, in order, a first site-specific recombination site (*attR*3), a negative selection marker (*Dpn*I), a first positive

selection marker (CmR), a second site-specific recombination site (*attR*1) and a second positive selection marker (ApR).

Support for the nucleic molecule of claim 139, is found, *inter alia*, in Figure 2D, which shows a map of the pEZCcoint plasmid. The pEZCcoint plasmid is a nucleic acid molecules which comprises, in order, (a) an origin of replication, (b) a first positive selection marker (amp), (c) a first site-specific recombination site (an *att*R site), (d) a second positive selection marker (kan), (e) a third positive selection marker (cam), and (f) a second site-specific recombination site (an *att*L site), wherein the first positive selection marker, the second positive marker and the third positive selection marker are different from each other.

Support for dependent claims 114-116, 126-128 and 140-142, directed to the use of *lox* sites and *att* sites, is found, *inter alia,* at page 18, line 20 of the specification.

Support for dependent claims 117 and 131, directed to the use of multiple cloning sites, is found, *inter alia*, in Example 1 (page 33, line 1.).

Support for dependent claims 118-119, 132-133 and 144-145, directed, in part, to vectors and expression vectors is found, *inter alia*, at page 17, line 17, through page 18, line 2, and Example 6, part 1 of the specification.

Support for dependent claims 120, 134, and 146, where positive selections markers are antibiotic resistance genes, is found, *inter alia*, at page 14, line 26, through page 15, line 15, of the specification.

Support for dependent claims 121, 135 and 147, directed to specific antibiotic resistance genes, is found, *inter alia*, in Figures 2A, 2B and 3B which disclose plasmids with multiple different antibiotic resistance genes.

Support for dependent claim 122, where the first and second positive selection markers are different antibiotic resistance genes, is found, *inter alia*, in Figures 2D and 3F, where plasmids having multiple different antibiotic genes are disclosed.

Support for dependent claims 123 and 136, directed to the second positive selectable marker being a chloramphenicol resistance gene, is found, *inter alia*, in Figure 4E, where the SP6 promoter, a *lox*P site and and chloramphenicol resistance gene are shown in order.

Support for dependent claims 124, 137-138 and 148-149, directed to host cells, is found, *inter alia*, at page 17, lines 17-20 of the specification.

Support for dependent claims 129 and 130, directed in part to the use of restriction endonuclease sites as selection markers is found, *inter alia*, at page 16 line 15 of the specification.

Therefore no new matter is added.

35 U.S.C. § 102

Claims 35-36, 35-49, 69, 72, 75, 79-82, 97, 99, 101-102, 107-108 and 110-112 stand rejected under 35 U.S.C. § 102(b), over Fukushige, S. *et al.* (*Proc. Natl. Acad. Sci. 89*:7905-7909 1992) (Office action, page 3.).

Claims 39, 43, 47-49, 79, 81, and 101-102 stand rejected under 35 U.S.C. § 102(e) over Wahl *et al.* (U.S. Patent No. 5,677,177) (Office Action, page 7.) Applicants respectfully disagree.

Solely to advance prosecution and without admitting to the appropriateness of the pending rejections, Applicants have canceled claims 35, 36, 38-54, 58-66, 69-75, 77, 79-88, 90-93 and 95-112 herein and added new claims 113-148. Applicants reserve the right to pursue the subject matter of claims 35, 36, 38-54, 58-66, 69-75, 77, 79-88, 90-93 and 95-112 in continuing applications.

Claims 35-36, 35-49, 69, 72, 75, 79-82, 97, 99, 101-102, 107-108 and 110-112 are canceled herein rendering the rejection over Fukushige *et al.* moot. Claims 39, 43, 47-49, 79, 81, and 101-102 are canceled herein rendering the rejection over Wahl *et al.* moot. As amended herein, new independent claims 113, 125 and 137 recite nucleic acid molecules comprising particular arrangements of site-specific recombination sites, selection markers and promoters among other features. Neither Fukushige *et al.* or Wahl *et al.* disclose such molecules and therefore none of the cited references anticipate the new independent claims 113, 125 and 137. Applicants respectfully request reconsideration and withdrawal of the rejection.

U.S.C. § 103(a)

Claims 35-36, 38-51, 65-66, 69-75, 79-86, 92-93, 95-103 and 107-112 stand rejected under 35 U.S.C. § 103(a), over Fukushige *et al.* and Wahl *et al.* in view of Lenski *et al.* (*J. Bact. 176*:3140-3147 1994). (Office action, page 9.)

Claims 35-36, 38-54, 58-66, 69-75, 77, 79-88, 90-93 and 95-112 stand rejected under 35 U.S.C. § 103(a), over Fukushige *et al.*, Wahl *et al.* and Lenski *et al.*, in view of Griffiths *et al.* (U.S. Patent No. 5,962,255). (Office action, page 10.). Applicants respectfully disagree.

Solely to advance prosecution and without admitting to the appropriateness of the pending rejections, Applicants have canceled claims 35, 36, 38-54, 58-66, 69-75, 77, 79-88, 90-93 and 95-112 herein and added new claims 113-134. Applicants reserve the right to pursue the subject matter of claims 35, 36, 38-54, 58-66, 69-75, 77, 79-88, 90-93 and 95-112 in continuing applications.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met. (*See* Manual of Patent Examining Procedure (MPEP) § 2142 (eighth edition, revision 5, August 2006).) First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

As amended herein, new independent claims 113, 125 and 137 recite nucleic acid molecules comprising particular arrangements of site-specific recombination sites, selection markers and promoters among other features. None of Fukushige *et al.*, Wahl *et al.*, Lenski *et al.*, or Griffiths *et al.*, alone or in combination, teach or suggest all the features of theses molecules.

Therefore, Applicants respectfully submit that a *prima facie* case of obviousness based on the disclosures of the cited references has not been established. Reconsideration and withdrawal of the rejection of pending claims 113-148 under 35 U.S.C. § 103(a) is therefore respectfully requested.

Conclusion

All of the stated grounds of rejection have been properly traversed or otherwise overcome. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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